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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,375	05/10/2005	Yuman Fong	08582/014002	5371

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
HAMA, JOANNE	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,375	FONG ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-14,22,23 and 28* is/are pending in the application.

4a) Of the above claim(s) *14,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-13 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 12, 2006 has been entered.

Claims 14, 22, 23 are withdrawn. Restriction was made final, December 28, 2005. Claims 2, 15-21, 24-27 are cancelled. Claim 1 is amended. Claim 28 is new.

Claims 1, 3-13, 28 are under consideration.

It is noted that the amendment to the claims does not comply with 37 CFR 1.121(c). Applicant has indicated that claims 14, 22, 23 are either "previously presented" or "original." However, these claims are "withdrawn" and should be labeled as such. Applicant must comply with the rules set forth in MPEP 714, or risk non-entry of amendments.

It is noted that the Examiner of record has changed.

Withdrawn Rejections

35 U.S.C. § 102

Applicant's arguments, see pages 9-11 of Applicant's response, filed October 12, 2006, with respect to the rejection of claims 1-3, 6, 8, 9, 12, 13 as being anticipated by

Molnar-Kimber, US Patent 6,428,968 have been fully considered and are persuasive. Applicant indicates that Molnar-Kimber does not describe administration of virus to sites of surgical resection. The rejection of claims 1, 3, 6, 8, 9, 12, 13 has been withdrawn. It is noted that the rejection of claim 2 is withdrawn as claim 2 is cancelled.

35 U.S.C. § 103(a)

Applicant's arguments, see pages 9-11, filed October 12, 2006, with respect to the rejection of claims 1-3, 6, 8, 9, 12, 13 as being obvious over Molnar-Kimber et al., US Patent 6,428,968, in view of Wong et al., 2001, have been fully considered and are persuasive. Applicant indicates that Molnar-Kimber does not describe administration of virus to sites of surgical resection (Applicant's response, page 9). The rejection of claims 1, 4, 6, 8, 9, 12, 13 has been withdrawn. It is noted that the rejection of claim 2 is withdrawn as claim 2 is cancelled.

Applicant's arguments, see pages 13-14 of Applicant's response, filed October 12, 2006, with respect to the rejection of claims 1, 3-5 as being obvious over Cole et al. US Patent 5,162,231, in view of Molnar-Kimber et al. US Patent 6,428,968, and in view of Johnston et al., 2001 have been fully considered and are persuasive. Applicant indicates that Molnar-Kimber does not teach administration of herpes to the site of surgical excision. The rejection of claims 1, 3-5 has been withdrawn.

Maintained/New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6, 8-13 remain rejected under 35 U.S.C. 102(e) as being anticipated by Fong et al., US 2002/0071832, for reasons of record, December 28, 2005 and July 7, 2006.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Applicant's arguments filed October 12, 2006 have been fully considered but they are not persuasive.

Applicant indicates that the Fong publication suggests the use of surgery to remove a tumor and inoculation of viruses into the resection site, to ensure destruction of any remaining tumor cells (Fong et al., parag. 36). Thus, the purpose of the method proposed in the Fong publication is to destroy tumor cells at the site of resection. Applicant indicates that in contrast, the presently amended claims specify the treatment

of metastases, which, by definition, are not at the site of resection. Applicant indicates that although the instant methods are similar to those proposed in the Fong publication, these steps are carried out for different purposes: the treatment (the present application) vs. destruction of resection site tumor cells (the Fong publication) (Applicant's response, pages 6-7). In response, this is not persuasive because regardless of what Fong et al. intended to be the end result, Fong et al. teach the claimed method steps. That is, while Fong et al. may have intended one particular result of their method described in their publication, the fact that the same method steps have other, not-yet-known effects anticipate the claimed invention. See MPEP 2112. This is because any of the effects caused by the method described by Fong et al. are inherent to the method.

> It is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. *In re Woodruff*, 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed.Cir. 1990); *In re Swinehart*, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and *Ex Parte Novitski*, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993).

While Applicant indicates that it is established in the law that "new uses of known products or processes are indeed patentable subject matter" (Applicant's response, page 6), this is not persuasive because there is no new use of the known process. Fong et al.'s process always had the ability to treat metastatic cells, whether or not Fong et al. realized it at the time of publication.

Applicant indicates that the methods of the present claims provide treatment options for patients for whom treatment regimens based solely on surgical excision of

tumors and destruction of tumor cells in the tumor bed would not have been considered sufficient. For example, treatment of tumors found to have metastasized or tumors having a high propensity to metastasize would not be effectively treated by an approach only focusing only on the site of excision. In response, this is not persuasive because claim 1 drawn to a method of treating metastases by administering herpes virus to the site of surgical resection. If Applicant indicates that it is not effective to treat metastases by focusing only on the site of excision, then claim 1 is not enabled. In addition to this, the specification teaches that, "(t)his study investigates the use of an attenuated, replication-competent, oncolytic herpes simplex virus (NV1023), both to treat a primary tumor by direct injection and to travel through the lymphatic system to treat metastatic tumors within the lymph nodes draining lymph from the site of primary cancer (specification, page 10)," which indicates that the treatment of primary cancer by direct injection must also treat metastatic cancer in the lymph nodes. If it is not effective to treat metastases by focusing only on the site of excision, then the specification does not provide an enabling disclosure.

Applicant indicates that treatment of metastases by administration of a virus to a site of tumor resection represents a new use of a method including tumor excision and virus administration to the excision site and can be use with a very select patient population that would not be treated with local methods alone (Applicant's response, page 8, 2nd parag.). In response, this is not persuasive because as described above, the method steps were already described by Fong et al. and while it may be that a new

discovery is made upon the already characterized method, this does not make the claimed method novel (MPEP 2112).

Applicant indicates that the nature of the targeted cells of the claimed method and that taught by Fong et al. are different. In particular, tumors having metastatic potential generally are highly heterogenous, and it is only certain cells within such tumors that have the capability to successfully form metastases, due to their unique abilities to overcome substantial obstacles to metastases. Applicant refers to the teachings of Fidler et al. for support (Applicant's response, page 8, 3rd parag.). In response, it is not entirely clear what argument is being presented. If the argument is that the instant invention is distinct from that of Fong et al. because the instant invention is drawn specifically to treating metastases, and that metastatic cells are highly heterogenous (e.g. see Fidler et al.), then the specification does not provide an enabling disclosure for treating metastatic cells in lymph nodes because the instant disclosure teaches treatment of mice implanted with a homogenous cancer cell line, SCC VII (specification, page 10).

Applicant indicates that tumor cells that form viable metastases may represent 1% or less of tumor cells that leave the site of a primary tumor. Applicant indicates Schirrmacher as support. Applicant indicates that only a fraction of the cells of a primary tumor leave the tumor and only a very small portion of these leaving cells form viable metastases. It thus follows that most cells within a tumor do not and likely cannot form metastases. Applicant indicates that these latter cells are the target of the method mentioned in the cited reference: cells that may, if left in the tumor bed, continue to

grow and form another tumor at the site of resection. The other, more specialized and rare cells, which may form metastases (and which are the subject of the present claims), are not mentioned in the cited reference (Applicant's emphasis, Applicant's response, page 9, 1st parag.). In response, Applicant's response is not persuasive because Applicant's arguments appear to indicate that the cells used by Fong et al. form tumors, but are not metastatic. In response, Fong et al.'s cells are metastatic; note that the OCUM-2MD3 cells seeds a variety of organ types (Fong et al., parag. 99) and that the art teaches that OCUM-2MD3 cells are metastatic (e.g. see Hippo, 2001, Cancer Research, 61: 889-895, abstract). Alternatively, if Applicant is indicating that the cells used by Fong et al. only form tumors at the site of resection (which the Examiner has interpreted to mean in the same tissue), then Applicant's argument is not persuasive because the cells used by Fong et al. metastasize a variety of organs and claim 1 does not require metastasis to other organs.

As such, the rejections as they apply to the claims remain. The rejection of claim 2 is withdrawn as claim 2 is cancelled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fong et al., US 2002/0071832, in view of Wong et al., 2001, Human Gene Therapy, 12: 253-265, for reasons of record, December 28, 2005 and July 7, 2006.

Applicant's arguments filed October 12, 2006 have been fully considered but they are not persuasive.

Applicant indicates that the present claims now specify the treatment of metastases, rather than the prevention or treatment of metastases. Further, Fong et al. do not teach treatment of metastasis; rather Fong et al. teach the destruction of tumor cells at the site of resection, to prevent re-growth of tumor cells and reformation of a tumor at the site of resection (Applicant's response, page 11). In response, Applicant indicating that the claims are now drawn only to treating and not including preventing, is not persuasive. "Treating" is a broad term and is not limited to having a disease and using methods to ameliorate it. Note, for example, that prophylaxis is a form of treatment wherein treatment steps are used to prevent disease or a disorder (Random

House Unabridged Dictionary (first entry), 2006 [retrieved on 2007-01-30]. Retrieved from the Internet:< URL: http://dictionary.reference.com/browse/prophylaxis >, pages 1-4, page 2, "prophylatic treatment"). As such, while the term "preventing" has been deleted from the claims, "treating" encompasses methods of preventing.

Applicant indicates that tumors including cells that have the potential to metastasize are highly heterogenous (Applicant's response, page 12). In response, as discussed above, it is not entirely clear what Applicant's argument is regarding this statement. If the argument is that the instant invention's disclosure and Fong et al.'s disclosure are distinct because Fong et al. do not use a cancer model that exhibits spontaneous metastases, then the instant invention disclosure is incomplete and not enabled because nothing in the specification teaches that the claimed method treats spontaneous metastases because the example in the specification depends on a cancer mouse model, wherein the cancer is seeded by a cancer cell line. In addition to this issue, nothing in the specification teaches that there is a difference between metastases that occurs spontaenously and metastases that occurs in an animal model that the claimed invention is unique for spontaneous metastases.

Thus, the rejection as they apply to the claims remains.

Claims 1, 3-6, 8, 9, 28 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Kooby et al., 1999, FASEB J. 13: 1325-1334, as evidenced by Rodgers and McCall, 2000, British Journal of Surgery, 87: 1142-1155.

Kooby et al., teach that rat models of hepatic micrometastases were given portal infusions of G207 (a replication competent type-1 herpes simplex virus) 7 days after splenic tumor challenge. G207-treated rat livers contained fewer nodules than PBS-treated rats (Kooby et al., page 1329, 2nd col. parag. under "Treatment of hepatic metastases with regional infusion of G207").

While Kooby et al. do not teach that the rats had tumors resected from their liver, Kooby et al. teach that the best treatment for colorectal cancer patients who have liver metastases is resection of the liver. Kooby et al. also teach that two-thirds of those who undergo successful resection, however, experience recurrence, presumably from microscopic residual disease. Kooby et al. teach that their method of using herpes virus can be used to improve outcome in these cases (Kooby et al., page 1325, 2nd col., 1st parag.).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to resect metastatic tumors in the livers of patients and to also administer G207 to the site of resection.

One having ordinary skill in the art would have been motivated to resect metastatic tumors in liver and to administer G207 because Kooby et al. teach that resection of tumor is the best treatment for patients who have liver metastases, that G207 was shown to reduce the number of tumor nodules in the liver of rat models, and that administration of G207 could be used to improve the outcome of patients who have residual disease following resection.

There would have been a reasonable expectation of success given teachings of Kooby et al. who indicate that resection of the liver is the best treatment for patients who have liver metastases and that G207 can be used to reduce the number of nodules in a rat cancer model.

It is noted that while Kooby et al. are silent as to whether the disease models exhibit any metastases in lymph nodes, the art at the time of filing teach that colorectal cancer, in addition to metastases in the liver can also have metastases in hepatic lymph nodes (Rodgers and McCall, page 1142, 1st col.). Given that the steps taught by Kooby et al. are the same as those of the claims, an artisan would have arrived at the claimed invention of treating metastases in lymph nodes.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER